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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/520,248	03/07/00	ABGRIGNANI S	CHIR-0234

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EXAMINER	
TUNG, M	
ART UNIT	**PAPER NUMBER**
1644	7

DATE MAILED: 04/24/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/520,248	Abgrignani
Examiner	**Art Unit**
Mary B. Tung	1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Feb 5, 2001*

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1, 3-6, and 10-12* is/are pending in the applica

4a) Of the above, claim(s) _____ is/are withdrawn from considera

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1, 3-6, and 10-12* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirem

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☒ Certified copies of the priority documents have been received in Application No. *08/776,259*.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 5

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

Specification

1. On page 13 of the specification, the Applicants replaced Table 1 in the paper filed 2/5/2001, Paper No. 6, to correct the headings for each column that appeared to be out of alignment. However, the amendment is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: in the second line of Table 1, the new Table omits the phrase "plus IL-6", which omission changes the scope of the disclosure and thus is new matter.

Applicants are required to cancel the new matter in the reply to this Office action, or to provide evidence of support in the original specification or claims as filed.

Abstract

2. It is acknowledged that the Applicants have provided an Abstract of the Disclosure as required by *37 C.F.R. § 1.72(b)*. However, the amendment is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: the phrase "in the absence of antigen," changes the scope of the disclosure and thus is new matter.

Applicants are required to cancel the new matter in the reply to this Office action, or to provide evidence of support in the original specification or claims as filed.

Claim Objections

3. It is acknowledged that Applicants submitted clean copies of the claims since claims 8-11 had text missing due to photocopying. Therefore, the objection is withdrawn.

Claim Rejections - 35 U.S.C. § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his invention.

5. Claims 5 and 6 are rejected under *35 U.S.C. § 112*, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

6. In claims 5 and 6 it is unclear to what the recited dosages refer. It is unclear whether for in vivo usage, a dosage of 100U/ml of IL-2 the concentration of IL-2 in the dose

administered to a subject, or whether the concentration of IL-2 is in the blood or tissue fluid following administration and distribution into these compartments.

7. Applicant's arguments filed in Paper No. 6 have been fully considered but they are not persuasive.

The Applicants argue that the dosages recited in claims 5 and 6 would be understood by one of skill in the art, in light of the specification. However, it is not clear to the Examiner that one of skill in the art would understand what dosage the Applicants intend. The Applicants are invited to direct the Examiner to the location in the specification to which one of skill in the art would refer. The rejection is therefore maintained.

Claim Rejections - 35 U.S.C. § 102

8. The following is a quotation of the appropriate paragraphs of *35 U.S.C. § 102* that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the Applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the Applicant for patent.

9. Claims 1, 3-6 and 10-12 stand rejected under 35 U.S.C. 102(b) as being anticipated by Chong, (U.S. Patent 4,879,111).

10. Chong discloses a method of administration of IL-2 and TNF-alpha for treatment of infections. The instant claims do not exclude contact of T cells of a subject with an infection with the combination of IL-2 and TNF-alpha. Although the dosages Applicant intends to use in vivo are unclear for the reasons discussed above in the rejection under 112/2 the dosages given in column 5 of the Chong appear to be comparable to the dosages recited in claims 5 and 6. The instant claims do recite "antigen independent activation of T cells" but this term does not distinguish over the prior art methods as any effects of IL-2 or TNF-alpha on T cells would be inherent to the prior art methods because they teach exactly the same method step: contacting T cells with IL-2 and TNF-alpha.

11. Applicants argue that "inherency may not be established by probabilities or possibilities; nor the mere fact that a certain thing may result from a given set of

circumstances sufficient to establish inherency." The Applicants also argue that "[u]nlike Chong and Zimmerman, et al., Applicant's claims do not require, inter alia, that TNF and IL-2 be administered in synergistically effective amounts." This argument is found unpersuasive because the claims do not exclude the teachings of Chong and Zimmerman and recite no limitations concerning synergistic effects of the combination of cytokines. Additionally, where the Patent Office has reason to believe that a functional limitation asserted to be critical for establishing novelty in the claimed subject matter may be an inherent characteristic of the prior art, it has the authority to require the Applicant to prove that the subject matter shown in the prior art does not possess the characteristics relied on. In re Schreiber, 44 USPQ2d 1429 (Fed. Cir. 1997).

12. Claims 1, 3-6 and 10-12 stand rejected under 35 U.S.C. 102(e) as being anticipated by Zimmerman et al. (U.S. Patent 5,425,940).

13. Zimmerman et al. disclose administration of a combination of IL-2 and TNF-alpha for treatment of tumors, see abstract. The dosages describe in col. 6 of the cited patent appear to fall within the same ranges as the dosages of IL-2 and TNF-alpha recited in instant claims 5 and 6.

14. Applicants argue that "inherency may not be established by probabilities or possibilities; nor the mere fact that a certain thing may result from a given set of circumstances sufficient to establish inherency." The Applicants also argue that "[u]nlike Chong and Zimmerman, et al., Applicant's claims do not require, inter alia, that TNF and IL-2 be administered in synergistically effective amounts." This argument is found unpersuasive because the claims do not exclude the teachings of Chong and Zimmerman and recite no limitations concerning synergistic effects of the combination of cytokines. Additionally, where the Patent Office has reason to believe that a functional limitation asserted to be critical for establishing novelty in the claimed subject matter may be an inherent characteristic of the prior art, it has the authority to require the applicant to prove that the subject matter shown in the prior art does not possess the characteristics relied on. In re Schreiber, 44 USPQ2d 1429 (Fed. Cir. 1997).

Claim Rejections - 35 U.S.C. § 103

15. The rejection of claims 1, 3-6 and 10-11 under 35 U.S.C. 103(a) as being unpatentable over Chong, (U.S. patent 4,879,111) in view of Paul, Fundamental Immunology (1993) is hereby withdrawn in light of the teachings by Paul, 1999, Fundamental Immunology, supplied by Applicants.

16. The rejection of claims 1, 3-6 and 10-11 under 35 U.S.C. 103(a) as being unpatentable over Zimmerman, et al., (U.S. patent 5,425,940) in view of Paul, Fundamental Immunology (1993), is hereby withdrawn in light of the teachings by Paul, 1999, Fundamental Immunology, supplied by Applicants. .

Double Patenting

17. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

18. A timely filed terminal disclaimer in compliance with 37 C.F.R. 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 C.F.R. 1.130(b).

19. Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 C.F.R. 3.73(b).

20. Claims 1 and 3-6 and new claim 12 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent No. 6,074,635.

21. Although the conflicting claims are not identical, they are not patentably distinct from each other. Although the amendment of Paper No. amended the claims to recite *in vivo* methods, one of ordinary skill in the art, given the *in vitro* methods claimed in the '635 patent, would have been motivated to use the taught methods *in vivo*, because one of ordinary skill in the art would recognize that treatment could be effected without the necessity of the manipulation of cells *ex vivo*. Additionally, the '635 patent teaches the same dosages and the claims are directed to methods of using the combination of IL-2 and TNF-alpha to activate T cells independently of antigen.

The following new grounds for rejection are necessitated by amendment:

Claim Rejections - 35 U.S.C. § 112

22. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

23. Claims 1, 3-6 and 10-12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 1 is not supported by the specification or by the claims as originally filed. There is no support in the specification or claims as originally filed for the recitation of the phrase "in the absence of antigen," which changes the scope of the disclosure and thus is new matter. There is no written description of the claimed invention in the specification or claims as originally filed. Thus the claimed invention constitutes **new matter.** The Applicants are invited to provide evidence of support for the recitation in the original specification or claims as filed.

24. Claim 10 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

25. Claim 10 is dependent upon claim 9, which was cancelled in Paper No. 6.

Allowable Subject Matter

26. No claim is allowed.

Conclusion

27. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. 1.136(a).

28. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory

period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

29. Papers related to this application may be submitted to Group 1640 by facsimile transmission. Papers should be faxed to Group 1640 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). THE CM1 FAX CENTER TELEPHONE NUMBER IS (703) 305-3014 or (703) 308-4242.

30. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Mary Tung whose telephone number is (703)308-9344. The Examiner can normally be reached Tuesday through Friday from 8:30 am to 6:00 pm and on alternating Mondays. A message may be left on the Examiner's voice mail service. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1640 receptionist whose telephone number is (703) 308-0196.

David A. Saunders

DAVID SAUNDERS
PRIMARY EXAMINER
ART UNIT ~~182~~ 1644

April 23, 2001
Mary B. Tung, Ph.D.
Patent Examiner
Group 1640